more accurate functional forms for main chain torsions in the future development of force field.

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798-Pos Board B578

Molecular Dynamics Simulation of Protein Crystal with Polarized Protein-Specific Charge

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The polarized force field model is indispensable in the simulation of protein crystal due to the particular electrostatic environment which is different from water solution or membrane. The polarized protein-specific charge (PPC) is fitted from in situ linear scaling quantum mechanical calculations of protein. The atomic charge for each residue is determined by its conformation and its location in the protein. Therefore, it gives a more accurate delineation of charge distribution in protein than the mean-field charge schemes in pairwise force fields do. Two 250 ns molecular simulations are carried out to study the structure and dynamics of crystal toxin protein II from the scorpion Androctonus australis Hector employing PPC, as well as the standard AMBER99SB force field, to investigate the effect of electrostatic polarization on the simulated crystal stability. Results show that PPC provides more reliable description of the monomers in the unit cell as well as the lattice in supercell with much smaller RMSDs and more realistic lattice atomic fluctuations. Most of the interactions at the interfaces among the protein units in the X-ray structure are well preserved, underscoring the important effect of polarization on maintaining the crystal stability.

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799-Pos Board B579

Extension of the CHARMM General Force Field to Linked Nitrogen-Containing Hetreroaromatic Rings

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The empirical CHARMM additive all-atom force field has been widely used for proteins, nucleic acids, lipids and carbohydrates, with the CHARMM General Force Field (CGenFF) portion of the force field specifically developed for chemical groups present in drug-like molecules. To more accurately treat linked nitrogen-containing heteroaromatic rings CGenFF was extended to molecules such as bi-pyridine, bi-pyrimidine, and bi-pyrrole. Target data include QM data for geometries, vibrations and dihedral potential energy scans (PES) as well as interactions with water. A total of 12 additional compounds were parameterized. To achieve adequate optimization it was necessary to introduce new atom types for selected linker atoms. A detailed comparison of the QM and MM data for the optimized parameters will be presented along with application of the model in MD simulations.

800-Pos Board B580

Phase Diagram of Lipid-Cholesterol Mixture: Comparison between Different Force Fields

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Molecular Dynamics simulations have shown to be a reliable tool for the understanding of biological processes at molecular level. The modelling of lipid bilayers with this technique is a common practice nowadays, leading to information on the behavior of such a complex systems. As in any other theoretical approach, validation regarding the experiments is required. In this work we analyse the behavior of different properties like thickness and lateral diffusion along the phase diagram of a mixture of POPC and cholesterol. We compare the results of different force fields (Berger, Charmm36 and Slipids) implemented in the GROMACS package. The results show the key role of the force field in the reproduction of the experimental behavior of the properties along the phase transitions. Only an ab-initio refined potential was able to do this.

801-Pos Board B581

Non-Markovian Analyses for Extracting Long-Time Behavior from Molecular Simulation Trajectories

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We address the question of how to analyze trajectory data when configuration space is divided into non-Markovian regions, noting that truly Markovian states may be difficult to delineate in some systems based on finite data. We build on our recent finding that with sufficient history information, unbiased equilibrium and non-equilibrium observables can be obtained even for arbitrary non-Markovian divisions of phase space [Suarez et. al., JCTC 2014, 10, p2658]. With the goal of predicting long-time behavior from sets of short trajectories, we now investigate several approximate non-Markovian estimators for rates using varying amounts of history. The analyses are applied to toy models as well as several proteins previously studied by μsec−msec scale atomistic simulations [Lindorff-Larsen et. al., Science 2011, 334, p517].

802-Pos Board B582

New Developments in the Collective Variables Module: More Flexible, More Interactive

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The collective variables module (colvars) is a software component integrated with molecular simulation and analysis programs. It implements reusable functions to reduce the dimensionality of complex chemical and biophysical systems, and a set of algorithms for enhanced sampling and statistical analysis. It is freely available in community programs for molecular dynamics such as NAMD and LAMMPS, and now also in the widely used analysis program VMD. We here present several innovations that expand the usefulness inside and outside the molecular dynamics community. It is now possible to add new functions and new algorithms via popular scripting languages (Tcl and Python), both in the analysis stage and during a simulation. Scientists involved in fields such as virtual drug screening, force field development and protein design benefit from specific features that maximize automation and flexibility. The existing multiple-replicas parallelization, previously available for metadynamics and Hamiltonian exchange, is also extended to the ABF method (contribution by J. Comer and C. Chipot). Parallelization of the collective variables' functional form allows for the study of computationally challenging problems, such as phase transition in membranes. The colvars module is an open development effort, which builds upon feedback and contribution from its community of users.

803-Pos Board B583

Parametrization of Halogen Bonds in the CHARMM General Force Field

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A halogen bond is a non-covalent, highly directional interaction between a halogen atom and another electronegative atom. The origin of this interaction is the formation of a small region of positive charge opposite the covalent bond to the halogen called the "sigma hole." As the non-polarizable additive force fields are based on point charges, they typically do not describe this interaction due to halogen atoms usually bearing a negative charge, thereby having unfavorable interactions with electronegative atoms. Within the framework of additive force fields, the simplest strategy to overcome this problem is to attach a virtual particle to the halogen that bears a point charge. In this study, we extend the additive CHARMM General Force Field to include such interactions in model systems Phenyl-R, with R being Cl, Br or I. The parameters of the models (ie. charges and LJ parameter of the halogen and virtual particle and the virtual-particle-halogen distance) were tuned to reproduce the orientation dependence of QM interaction energies with water and acetone and experimental pure solvent and aqueous free energies of solvation data. Furthermore, once parameters for the monohalogenated compounds were derived, we extended the parametrization to include phenyl rings with up to three halogens in all possible positions. Finally, the resulting parameters